REMARKS

I. Status of the Claims

Claims 1, 2, and 7-27 are pending, with claims 1 and 27 being independent.

II. Period for Reply Reset

Applicant gratefully acknowledges the Examiner for resetting the period for reply. *See* Request for Restarting Period for Reply dated February 9, 2005.

III. Claim Rejection under 35 U.S.C. § 103

Claims 1, 2, and 7-27 have been rejected as allegedly being unpatentable over *Griffiths et al.* (BRYAN GRIFFITHS & DENIS LOOBY, *Scale-Up of Suspension and Anchorage-Dependent Animal Cells, in* 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 59 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997)) and *Pollard* (JEFFREY W. POLLARD, *Basic Cell Culture, in* 75 METHODS IN MOLECULAR BIOLOGY: BASIC CELL CULTURE PROTOCOLS 1 (Jeffrey W. Pollard & John M. Walker eds., 2d ed. 1997)). Final Office Action dated April 20, 2005, at 2. Applicant respectfully disagrees with this rejection.

A. Passage Number Is Relevant to Obviousness Question

On page 2 of the Final Office Action, the Examiner states: "Applicant now argues that the 'different passage number' limitation obviates the prior art rejection, however applicant's specification appears to indicate that the passage number is irrelevant (page 4, lines 20-22) and thus can not be considered an obvious distinction."

To the contrary, Applicant respectfully contends that passage number is highly "relevant" to the patentability of the pending claims. Viewed in the context of Applicant's disclosure, it is plain that Applicant has invented methods that break from the rigid and unnecessary adherence to passage number evident in the alleged prior art.

Without Applicant's invention, the production of biologicals such as viruses for vaccines requires the growth of a vast array of cells all having the same passage number. *See, e.g., Wiktor et al.,* U.S. Pat. No. 4,664,912, at col. 2, ll. 68-69; *see also* Applicant's specification at 1, ll. 15-20; and at 4, ll. 26-34. In that method, vessel upon vessel of cells all having the same passage number were prepared, and then seeded with virus for the production of vaccine. That created an enormous logistical problem of managing preproduction batches and harvesting the virus at the optimum time. Key to that method was the production number of the cells: the production number had to be the same for every production batch. As Applicant explains: "In classical serial production lines the number of doubling of the cells derived from the MWCS at the moment of harvest is known up front within certain limits. A maximum allowable generation number is set to the production system at the onset." Specification at 4, ll. 15-17.

Now, Applicant discloses methods that do not require strict adherence to production number. Indeed, "Production passage number (the number of cell passages used prior to production of the biological product), hence, is irrelevant within the limits set by ECB." Specification at 4, ll. 20-21. Production number according to the present invention is "irrelevant" in the sense that the same production number is no longer required in all production batches. As Applicant explains, "Once such ECB is fully

characterised one may allow to produce the product with cells at any passage number between MCB and ECB[.]" *Id.,* ll. 29-31. Therefore, a *different* passage number can be used in production batches, and in some embodiments, the logistical problems mentioned above can be lessened. Accordingly, Applicant claims "wherein the cells of the at least one first production batch have a passage number different from the cells of the at least one second production batch." Claim 27. Similarly, in claim 1, clause (f), Applicant claims "wherein the cells of the at least one production batch of c) have a different passage number than the cells of the at least one subsequent production batch of f)."

The Court of Appeals for the Federal Circuit and the United States Patent and Trademark Office require that during prosecution, claims receive their broadest reasonable interpretation. *See* M.P.E.P. § 2111 (*quoting In re Hyatt,* 211 F.3d 1367, 1372, 54 U.S.P.Q.2d (BNA) 1664, 1667 (Fed. Cir. 2000)). It is not reasonable to interpret "different" to mean "the same" in Applicant's pending claims. It is furthermore not reasonable to mentally excise that claim language from claims 1 and 27, and give it no meaning whatsoever.

Therefore, Applicant respectfully requests that the claim language respecting passage number be given its broadest reasonable interpretation, and be included in the patentability analysis.

B. Claimed Methods Are Patentable

Applicant respectfully contends that a *prima facie* case of obviousness has not been made against the pending claims.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. M.P.E.P. § 2143.

The cited documents, *Griffiths et al.* and *Pollard et al.,* do not teach or suggest that cells having different passage numbers can be used in production batches. *Wiktor et al.* reinforces that it is conventional to employ only the same passage numbers across all production batches.

> Preferably, in starting with the VERO working seed, a passage is effected in a 1 liter biogenerator. The cells are obtained by digestion with a very purified and diluted protease solution, then a passage is effected in a 5 liter biogenerator; then a new passage is effected in a 25 liter biogenerator; then a new passage is effected in a 150 liter biogenerator, and a last passage is effected with the use of a biogenerator of very large volume (for example 1000 liters), or a plurality of biogenerators of smaller volume (for example 150 liters), the inoculation by the virus being effected in this last passage.

Wiktor et al., U.S. Pat. No. 4,664,912, at col. 2, ll. 58-69.

The Examiner offers that "It would have been obvious at the time the invention was made to use a production batch with any passage number wherein the cells maintain the desired phenotype and/or production capabilities." Final Office Action at 2-3. The Examiner offers no support for this assertion. *See* M.P.E.P. § 2144.03 (requiring substantial evidence to support grounds of rejection). Moreover, that "any"

passage number might be used does not suggest that "different" passage numbers can be used.

Accordingly, Applicant respectfully contends that a *prima facie* case of obviousness has not been made. This rejection therefore should be withdrawn.

C. Claimed Methods Exhibit Unexpectedly Facile Production of Biologicals

As explained above, Applicant respectfully contends that a prima facie case of obviousness has not been made. Nonetheless, to further show that the claimed methods are patentable, Applicant points to the unexpected results of his useful, new, and non-obvious invention.

In at least some embodiments, "The method described allows high through-put production since the up scaling route from WCS to production cells can be very much shortened and much less bioreactors are needed since parallel production lines are not needed anymore." Specification at 3, l. 35 - 4, l. 2. *Contrast, Wiktor et al.* at col. 2, ll. 58-69. This can represent a significant savings in time, resource allocation, and money, resulting in smaller and better-controlled growth and harvesting processes for biologicals such as viruses and enzymes.

For these reasons, Applicant respectfully requests that the pending rejection be withdrawn and the pending claims be allowed.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this Response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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